UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

NOV 18 1983

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

TO: Jay Ellenberger, PM #25
Insecticide Branch
Registration Division (TS-767)

THRU: Robert B. Jaeger, Section Head
Review Section #1
Toxicology Branch/HED (TS-769) 11/3/83

SUBJECT: Chlorpyrifos-methyl
O, O-dimethyl-O-(3,5,6-trichloro-2-pyridyl
phosphorothioate, TOX #179AA 11/17/83

Petitioner: Dow Chemical Co. (letter of October 11, 1983)
OF2423.

Action Requested:

Review of proposed protocol for a subchronic delayed neurotoxicity study in laying hens.

Recommendation:

(Memo of October 27, 1983 from W. T. Edwards to R. E. Landolt). The Registrant is referred to the November 1982 guidelines for subchronic neurotoxicity studies as these represent current acceptable testing procedures. TB has the following recommendations with respect to the proposed protocol:

1. Page 3, Test Animals. Laying hens are specified in the guidelines and should be included in this protocol.

2. Page 9, Pathology. The proposed procedures should include in situ whole body perfusion, which has been omitted in the submitted proposal.

Background Information:

A proposed protocol for subchronic delayed neurotoxicity was initially discussed in the August 24, 1983 meeting with representatives of Dow Chemical Co. Eleven issues were covered in this meeting that were of concern to Dow Chemical Co. regarding the initation of the subchronic delayed neurotoxicity study. Except for the data on a four week neurotoxic probe study the issues of concern were covered in the November 1982 guidelines for subchronic delayed neurotoxicity testing (82-5). The data for the following prob study were presented initially in the August 24, 1983 meeting with a summation of the histopathologic evaluation included with the present request.

Toxicity Data Review:

4 week delayed neurotoxicity - Hen
Dow Chemical TXT:K-046193-(18) June 1983.

A. Procedure

"Chlorpyrifos-methyl (92%) was administered in corn oil by gavage to five laying hens per group at dosage levels of 0, 50, 100, 250, 500, 750 and 1000 mg/kg/day, 5 days/week for 4 weeks, for a total of 20 doses."

B. Results

1. Egg production
   By day 5 egg production stopped for dosage levels 1000, 750 and 500 mg/kg with reduced production reported for the 250 mg/kg level.

2. Signs of toxicity consisted of decreased activity at the 1000 mg/kg level at days 3 and 10 with ataxia reported for the 1000 and 750 mg/kg level by day 16.

3. Mean body weight
   A decrease in weight gain was reported for the 1000 and 750 mg/kg levels by the second week of the study.

4. Mortality
   Two animals died at the 1000 mg/kg level on days 15 and 24 respectively. One of these animals was reported to have died of pneumonia.

5. Histopathologic Evaluation
No microscopic lesions reported of the brain, spinal cord and peripheral nerve from any dosage level tested. A "loss of body fat depots:" was reported for the 1000 mg/kg level.

C. Conclusions:

1. Classification of data - Supplemental

a. Deficiency
This study was designed as a dose range finding study and was not intended to determine delayed neurotoxicity in the hen.

Ray Landolt November 3, 1983

Ray Landolt
Review Section #1
Toxicology Branch/HED(TS-769)

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